

REMARKS

Claims 1 and 3-24, as amended, appear in this application for the Examiner's review and consideration. Claims 1 and 14 have been amended to clarify the present invention by defining the orientation of the electrodes, support of which is found in the specification, e.g., FIGs. 9 and 10 as well as paragraphs [0022] and [0060] of the published application. Since no new matter is introduced by these changes, the amendment should be entered at this time.

Claims 1, 3, 5-7, 9, 12-17, 19, 22, and 23 have been rejected under 35 U.S.C. 103(a) as being unpatentable over a publication by Bramson et al. (Gene Therapy 10: 251-260, 2003; referred to hereafter as "Bramson") in view of U.S. Patent No. 6,302,874 to Zhang et al. (referred to hereafter as "Zhang"). Bramson disclosed a microporation technique whereby a vaporization process was used to remove tiny areas of the stratum corneum creating microscopic pores that enabled topical immunization (*see* abstract of Bramson). According to Bramson, microporation was preformed by the contact of electrically heated small-diameter wires (*see* right column on p. 258 of Bramson) with the skin surface. The small-diameter (80 μ m) wires according to Bramson were strapped over the edge of a ceramic substrate and electrically connected to the control circuitry via copper traces on each side of the substrate (*see* left column on p. 259 of Bramson). The control circuitry allowed for the precise control of the electrical current pulses that were passed through each wire (*see* left column on p. 259 of Bramson). The Examiner erred in stating that the system of Bramson comprises "a control unit which is adapted to apply electrical energy between two or more electrodes in the vicinity of skin, enabling ablation of the stratum corneum, thereby generating in the stratum corneum a plurality of micro-channels" (*see* page 4 of the pending Office Action; underline added for emphasis). According to Bramson, micropores were generated by virtue of thermal energy based on resistive heating of the wires, (*see* right column on p. 258 of Bramson). It should be understood that the microporation system of Bramson is characterized by the following features: (1) the wires were strapped over the edge of a ceramic substrate so that the wires were parallel to the skin surface; and (2) the electrical current passed through the wires only, not through the skin, heated the wires which thereby generated micropores. In contrast, the apparatus of the present invention comprises: (a) an electrode cartridge comprising a plurality of electrodes to be oriented generally perpendicularly to the skin with electrode ends in the vicinity of the skin (*see* FIGs. 9 and 10 of the application); and (b) a

main unit comprising a control unit which is adapted to apply electrical energy – via the skin - between two or more electrodes when the electrodes are in vicinity of the skin, typically generating current flow or one or more sparks, enabling ablation of stratum corneum in an area beneath the electrodes, thereby generating in the stratum corneum a plurality of micro-channels having a diameter of about 10 microns to about 100 microns and a depth of about 20 microns to about 300 microns. As noted, the electrodes of the present invention are perpendicular to the skin surface such that the electrical energy is applied between the electrodes (*see* paragraphs [0022] and [0060] of the published application). This electrical energy carried by electrical current is converted within the skin to heat, by virtue of the skin resistivity, which ablates the stratum corneum and thereby generates micro-channels (*see* paragraph [0067] of the published application). Thus, the heat according to the present invention is not generated in the electrodes which are conductive, but rather outside the electrodes when electrical current flows through the skin. Therefore, according to the present invention, it is not the heated wires that are parallel to and in contact with the skin surface which generate micro-channels. It is the electrical energy (current) that is delivered from the ends of the perpendicularly oriented electrodes into the skin which generates heat within the skin to form the micro-channels. In order to further distinguish the system of the present invention from the microporation system of Bramson, claims 1 and 14 have been amended to recite that the electrodes are oriented perpendicularly to the skin with electrode ends in the vicinity of the skin.

Zhang does not remedy the deficiencies of Bramson. Zhang teaches apparatuses for electroporation so as to create transient aqueous pathways (pores) in lipid bilayers (col. 2, ll. 65-66; col. 4, ll. 31-33 of Zhang). The apparatus according to Zhang comprises a mini pulse generator in electrical contact with an electrode (col. 10, ll. 30-34 of Zhang). The electroporation according to Zhang is achieved by pulsed electric fields, specifically electrostatic fields (FIG. 2; col. 9, ll. 61-63; col. 10, ll. 1-6; col. 10, ll. 14-16 of Zhang). Zhang further discloses transdermal delivery of L-ascorbic acid for cosmetic treatment of skin conditions (col. 3, ll. 54-61; col. 7, ll. 31-33 of Zhang). Moreover, the delivery of L-ascorbic acid according to Zhang is enhanced by applying an electric pulse having sufficient strength and duration to the composition so as to topically deliver L-ascorbic acid to the region of skin (col. 4, ll. 31-42; col. 7, ll. 10-18 of Zhang). Thus, even if one of ordinary skill in the art at the time the invention was made was to modify the patch of Bramson to a patch containing a cosmetic composition of

Zhang, he/she would only obtain a system which comprises a laptop computer, a microprocessor control circuitry, a three-axis stepper motor assembly with microporation tip holder. The microporation tip would comprise small-diameter wires strapped over the edge of a ceramic substrate and electrically connected to the control circuitry, which would allow for the control of the electrical current pulses to pass through the wires and heat the wires. As a result, the wires would heat up the skin surface and create lines of micropores on the patient's skin. The patch of Zhang comprising L-ascorbic acid would then be applied onto the skin where micropores are present. Thus, even combining the Bramson system with the patch of Zhang, one of ordinary skill in the art would not arrive at the presently claimed system which comprises: (i) an apparatus comprising: (a) an electrode cartridge comprising a plurality of electrodes to be oriented generally perpendicularly to the skin with electrode ends in vicinity of the skin; and (b) a main unit comprising a control unit which is adapted to apply electrical energy between the plurality of electrodes when said plurality of electrodes are in vicinity of the skin, typically generating current flow or one or more sparks, enabling ablation of stratum corneum in an area beneath the electrodes, thereby generating the plurality of micro-channels; and (ii) a cosmetic or dermatological composition comprising a water-soluble, poorly water-soluble or water insoluble cosmetic agent. In sum, claims 1 and 14 as well as their dependent claims 3, 5-7, 9, 12, 13, 15-17, 19, 22 and 23 are patentable over Bramson in view of Zhang. Therefore, the rejection should be withdrawn.

Claim 4 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Bramson in view of Zhang and further in view of U.S. Patent Application Publication No. 2002/0010414 to Coston (referred to hereafter as "Coston"). As explained above, the combination of Bramson and Zhang does not teach or suggest the presently claimed invention. The Examiner cites Coston as an attempt to remedy the failure of Bramson and Zhang to teach that the electrical energy is of radio frequency.

However, Coston does not remedy the deficiencies of Bramson in view of Zhang. Coston discloses methods and devices for transporting a molecule through a mammalian barrier membrane through electroporation of the membrane. Coston teaches various apparatuses for the electroporation methods, one of which comprises a housing, a current generator, a current controller, and a treatment electrode for electroporation in a mono-terminal operation (*see* paragraph [0067] and FIG. 1 of Coston). Another apparatus of Coston comprises a housing, an

electric current generator, an electric current controller, a treatment electrode for electroporation, and an indifferent electrode (*see* paragraph [0072] and FIG. 2a of Coston). Yet another electroporation apparatus of Coston is a bi-terminal apparatus with two treatment electrodes located very close to, but separated from, each other (*see* paragraph [0074] and FIG. 2b of Coston). The electric current according to Coston is driven from the treatment electrode to the membrane, and optionally to the indifferent electrode (*see* paragraph [0015] of Coston). The electric current may be a direct current or an alternating current. The frequency of the alternating current may be between 30 Hz to 10,000 kHz (*see* paragraph [0016] of Coston). Thus, combining the system of Bramson in view of Zhang, and further in view of Coston, one of ordinary skill in the art would obtain a system which comprises a laptop computer, a microprocessor control circuitry, a three-axis stepper motor assembly with microporation tip holder. The microporation tip would comprise small-diameter wires strapped over the edge of a ceramic substrate and electrically connected to the control circuitry, which would allow for the control of the radio frequency electrical current to pass through the wires and heat the wires. As a result, the wires would heat up the skin surface and create lines of micropores on the patient's skin. The patch of Zhang comprising L-ascorbic acid would then be applied onto the skin where micropores are present. Thus, even combining the Bramson system with the patch of Zhang and the frequency parameter of Coston, one of ordinary skill in the art would not arrive at the system recited in claim 4 which comprises: (i) an apparatus comprising: (a) an electrode cartridge comprising a plurality of electrodes to be oriented generally perpendicularly to the skin with electrode ends in vicinity of the skin; and (b) a main unit comprising a control unit which is adapted to apply radio frequency electrical energy between the plurality of electrodes when said plurality of electrodes are in vicinity of the skin, typically generating current flow or one or more sparks, enabling ablation of stratum corneum in an area beneath the electrodes, thereby generating the plurality of micro-channels; and (ii) a cosmetic or dermatological composition comprising a water-soluble, poorly water-soluble or water insoluble cosmetic agent. Therefore, the rejection of claim 4 over Bramson in view Zhang, and further in view of Coston should be withdrawn.

Claims 8, 10, 11, 18, 20, and 21 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Bramson in view of Zhang, and further in view of U.S. Patent No. 6,477,410 to Henley (referred to hereafter as "Henley"). As explained above, the combination of Bramson

and Zhang does not teach or suggest the presently claimed invention. The Examiner cites Henley as an attempt to remedy the failure of Bramson and Zhang to teach wherein the cosmetic agent is hydroquinone.

However, Henley does not remedy the deficiencies of Bramson in view of Zhang. Henley teaches a self-powered hand-held electrokinetic delivery device for self-administering a medicament. The hand-held device of Henley electrokinetically drives the medicament from an applicator into the treatment site (col. 6, ll. 50-54 of Henley). Henley discloses different medicaments including hydroquinone and antibacterial agents to be delivered electrokinetically. However, Henley does not disclose an apparatus comprising an electrode cartridge comprising a plurality of electrodes to be oriented generally perpendicularly to the skin with electrode ends in the vicinity of the skin; and a main unit comprising a control unit which is adapted to apply electrical energy between the plurality of electrodes when said plurality of electrodes are in the vicinity of the skin, typically generating current flow or one or more sparks, enabling ablation of stratum corneum in an area beneath the electrodes, thereby generating the plurality of micro-channels as recited and claimed in claim 1 as amended. Moreover, as explained above, Bramson and Zhang do not teach or suggest the presently claimed apparatus. Thus, even modifying the Bramson system with the patch of Zhang to apply the cosmetic agent hydroquinone as taught by Henley, one of ordinary skill in the art at the time the invention was made would not arrive at the presently claimed invention. Therefore, the rejection of claims 8, 10, 11, 18, 20 and 21 over Bramson in view of Zhang, and further in view of Henley should be withdrawn.

Claims 1, 4, and 14 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9, 23, 30, and 36 of copending application No. 10/597,431. It is respectfully submitted that claims 1 and 14 as amended are different from the claims of copending application No. 10/597,431. Moreover, as the copending application has not yet been examined and the present claims are allowable, the provision has not occurred and the nonstatutory obviousness-type double patenting rejection should be withdrawn.

Accordingly, it is believed that the entire application is in condition for allowance, early notice of which would be appreciated. Should the Examiner not agree, then a personal or telephonic interview is respectfully requested to discuss any remaining issues and expedite the eventual allowance of this application.

Respectfully submitted,

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